Claims

1. (Previously presented) A humanized anti-TAG-72 CC49 antibody comprising:

a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2, and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)1, a H-CDR2, and a H-CDR3,

wherein L-CDR3, H-CDR1, H-CDR2 and H-CDR3 comprise murine monoclonal CC49 antibody Complementarity Determining Regions (CDRs) and at least one of L-CDR1 and L-CDR2 are a human monoclonal LEN antibody L-CDR1 and L-CDR2,

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, as compared to a parental humanized CC49 antibody.

2. (Previously presented) The humanized antibody of claim 1, wherein L-CDR1 is the human monoclonal LEN antibody L-CDR1.

3. (Canceled)

3 4. (Previously presented) The humanized antibody of claim 1, wherein L-CDR2 is the human monoclonal LEN antibody L-CDR2.

5. (Canceled)

4 6. (Previously presented) The humanized antibody of claim 1, wherein both L-CDR1 and L-CDR2 are human monoclonal LEN antibody L-CDR1 and L-CDR2, respectively.

7-9. (Canceled)

5 10. (Previously presented) The humanized antibody of claim 1, wherein the parental humanized CC49 antibody comprises three L-CDRS and three H-CDRs of the murine monoclonal CC49 antibody, a variable light chain framework of a human monoclonal LEN antibody, and a variable heavy chain framework of a human monoclonal 21/28'CL antibody.

6 11. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:

a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2, and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)1, a H-CDR2, and a H-CDR3,

wherein ~~at least~~ L-CDR3, H-CDR1, H-CDR2 and H-CDR3 are of a murine CC49 monoclonal antibody ~~L-CDR3, H-CDR1, H-CDR2 and H-CDR3,~~ and ~~wherein~~ L-CDR1 and L-CDR2 are ~~murine CC49 antibody or~~ of a human monoclonal LEN antibody L-CDR1 and L-CDR2 respectively, and wherein at least one amino acid at position 60, 61, 62, or 64 in the murine CC49 H-CDR2 is replaced with an amino acid at a corresponding position in the human monoclonal 21/28'CL antibody,

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

7 12. (Previously presented) The humanized antibody of claim ~~11~~ 6, wherein an asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine.

8 13. (Previously presented) The humanized antibody of claim ~~11~~ 6, wherein a threonine at position 97 of the murine CC49 L-CDR3 is replaced with a serine.

14. (Canceled)

9 15. (Previously presented) The humanized antibody of claim 11, wherein L-CDR1 is a human monoclonal LEN antibody L-CDR1.

16. (Canceled)

10 17. (Previously presented) The humanized antibody of claim 11, wherein L-CDR2 is a human monoclonal LEN antibody L-CDR2.

18. (Canceled)

11 19. (Previously presented) The humanized antibody of claim 6, wherein both L-CDR1 and L-CDR2 are human monoclonal LEN antibody L-CDR1 and L-CDR2, respectively.

20. (Canceled)

12 21. (Previously presented) The humanized antibody of claim 6, wherein a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine.

13 22. (Previously presented) The humanized antibody of claim 6, wherein an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine.

14 23. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:

a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2, and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)1, a H-CDR2, and a H-CDR3,

wherein L-CDR3, H-CDR1, H-CDR2 and H-CDR3 are of a murine CC49 monoclonal antibody ~~L-CDR3, H-CDR1, H-CDR2 and H-CDR3,~~ and ~~wherein~~ L-CDR1 and L-CDR2 are ~~murine CC49 antibody or~~ of a human monoclonal LEN antibody L-CDR1 and L-CDR2 respectively, and wherein a threonine at position 97 in the murine CC49 L-CDR3 is replaced with a serine,

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

15 24. (Previously presented) The humanized antibody of claim 14, wherein at least one amino acid of positions 60, 61, 62, or 64 in the murine CC49 H-CDR2 is replaced with an amino acid at a corresponding position in the human monoclonal 21/28'CL antibody.

25. (Canceled)

16 26. (Previously presented) The humanized antibody of claim 14, wherein L-CDR1 is a human monoclonal LEN antibody L-CDR1.

27. (Canceled)

17 28. (Previously presented) The humanized antibody of claim 23, wherein L-CDR2 is a human monoclonal LEN antibody L-CDR2.

29. (Canceled)

18 30. (Previously presented) The humanized antibody of claim 23, wherein both L-CDR1 and L-CDR2 are human monoclonal LEN antibody L-CDR1 and L-CDR2, respectively.

31-33. (Canceled)

19 34. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:

a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2, and a L-CDR3; and a heavy chain Complementarity Determining (H-CDR)1, a H-CDR2, and a H-CDR3,

wherein ~~L-CDR1, L-CDR2,~~ L-CDR3, H-CDR1, H-CDR2 and H-CDR3 are of a murine CC49 antibody and L-CDR1 and L-CDR2 are of a human monoclonal LEN antibody L-CDR1 and L-CDR2 respectively, and

wherein (1) a threonine is at position 94 in the L-CDR3, or (2) a serine is at position 97 in the L-CDR3, or (3) a threonine is at position 94 and a serine is at position 97 in the L-CDR3,

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

20 35. (Currently amended) ~~The humanized antibody of claim 34,~~ A humanized anti-TAG-72 CC49 antibody comprising:

a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2, and a L-CDR3; and a heavy chain Complementarity Determining (H-CDR)1, a H-CDR2, and a H-CDR3,

wherein L-CDR3, H-CDR1, H-CDR2 and H-CDR3 are of a murine CC49 antibody and L-CDR1 and L-CDR2 are of a human monoclonal LEN antibody L-CDR1 and L-CDR2 respectively, and

wherein ~~the~~ a threonine is at position 94 in the L-CDR3,

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

36-37. (Canceled)

21 ~~38.~~ (Previously presented) A pharmaceutical composition, comprising a therapeutically effective amount of the humanized antibody of claim 1 in a pharmaceutically acceptable carrier.

39. (Canceled)

22 ~~40.~~ (Previously presented) A composition comprising a functional fragment of the humanized antibody of claim 1, wherein the functional fragment specifically binds TAG-72.

23 ~~41.~~ (Previously presented) The composition of claim 22 ~~40~~, wherein the fragment comprises an Fv, an Fab, or an $F(ab')_2$.

42-47. (Canceled)

24 ~~48.~~ (Previously presented) The humanized antibody of claim 2, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7.

25 ~~49.~~ (Previously presented) The humanized antibody of claim 3 ~~1~~, wherein the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

50. (Previously presented) The humanized antibody of claim 6, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7 and the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

51. (Previously presented) The humanized antibody of claim 11, wherein a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine.

52. (Previously presented) The humanized antibody of claim 11, wherein the amino acid at the corresponding position in the human monoclonal 21/28'CL antibody comprises an amino acid corresponding to position 12, 13, 14, or 16 of the amino acid sequence as set forth in SEQ ID NO: 11.

53. (Previously presented) The humanized antibody of claim 11, wherein the parental humanized CC49 antibody comprises three L-CDRs and three H-CDRs from the murine monoclonal CC49 antibody, a variable light chain framework from a human monoclonal LEN antibody, and a variable heavy chain framework from a human monoclonal 21/28'CL antibody.

54. (Previously presented) The humanized antibody of claim 15, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7.

55. (Previously presented) The humanized antibody of claim 17, wherein the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

56. (Previously presented) The humanized antibody of claim 19, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7 and the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

57. (Previously presented) The humanized antibody of claim 23, wherein the parental humanized CC49 antibody comprises three L-CDRs and three H-CDRs from the murine monoclonal CC49 antibody, a variable light chain framework from a human monoclonal LEN antibody, and a variable heavy chain framework from a human monoclonal 21/28'CL antibody.

58. (Currently amended) The humanized antibody of claim 24, wherein the amino acid at position 60 is a serine, the amino acid at position 61 is a glutamine, the amino acid at position 62 is a lysine, or the amino acid at position 64 is a glutamine~~the corresponding position in the human monoclonal 21/28'CL antibody comprises amino acid 12, 13, 14, or 16, respectively, of an amino acid sequence as set forth in SEQ ID NO: 11~~.

59. (Previously presented) The humanized antibody of claim 24, wherein an asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine.

60. (Previously presented) The humanized antibody of claim 24, wherein a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine.

61. (Previously presented) The humanized antibody of claim 24, wherein an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine.

62. (Previously presented) The humanized antibody of claim 24, wherein a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine.

63. (Previously presented) The humanized antibody of claim 26, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7.

64. (Previously presented) The humanized antibody of claim 28, wherein the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

65. (Previously presented) The humanized antibody of claim 30, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7 and the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

66. (Previously presented) The humanized antibody of claim 34, wherein the serine is at position 97 in the L-CDR3 from the murine CC49 antibody.

43 67. (Previously presented) The humanized antibody of claim 34, wherein the threonine is at position 94 in the L-CDR3 from the murine CC49 antibody and the serine is at position 97 in the L-CDR3 from the murine CC49 antibody.

44 68. (Previously presented) The humanized antibody of claim 1, wherein an asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine, a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine, an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine, and a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine.

45 69. (Previously presented) A kit comprising a container comprising the humanized antibody of claim 1 and instructions for using the humanized antibody to treat or detect a cancer cell expressing TAG-72.

46 70. (new) The humanized antibody of claim 68, wherein a threonine at position 97 of the murine CC49 L-CDR3 is replaced with a serine.

47 71. (new) The humanized antibody of claim 70, wherein the humanized antibody is radiolabeled.